

Original Paper

Clinical Practice of Two Measurements of Home Blood Pressure on Each Occasion in Patients with Chronic Kidney Disease

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Key Words

Home blood pressure · Self-measurement of blood pressure · Blood pressure variability · Chronic kidney disease · Hypertension

Abstract

Background/Aims: Although several guidelines propose two or three measurements of home blood pressure (HBP) on each occasion, the actual status of multiple measurements is not clear in the practical management of hypertension. We surveyed the details regarding two measurements of HBP in patients with chronic kidney disease (CKD). **Methods:** HBP was measured twice every morning and evening over 7 consecutive days in 175 CKD patients. The distribution of the differences between two BP values (2nd – 1st BP) and their association with BP parameters were evaluated. **Results:** The 2nd – 1st morning systolic BP (SBP) and diastolic BP (DBP) differences were -2.3 ± 4.1 and -0.4 ± 2.6 mm Hg, respectively. The proportion of 2nd – 1st morning SBP differences >0 mm Hg was 31.7% in a total of 1,195 measurements. Eighty patients (45.7%) had days with a difference ≤ -5 mm Hg and days with a difference ≥ 5 mm Hg in morning SBP during 7 days. The multivariate regression analysis of the SD values of 2nd – 1st morning SBP as a dependent variable showed that the SD value of the 1st morning SBP ($\beta = 0.65$, $p < 0.001$) was a significant determinant. **Conclusion:** Although the 2nd SBP was 2–3 mm Hg lower than the 1st SBP in the population as a whole, various differences were found for each subject during 7 days. 2nd – 1st BP variability might be associated with day-by-day 1st BP variability.

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Introduction

The measurement of home blood pressure (HBP) is popular in the management of hypertension in everyday practice. HBP has great advantages over clinical BP, including its reproducibility, exclusion of the white-coat effect, an association with target organ damage, and a

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better prognostic value [1–5]. Many BP data can easily be obtained during the course of a day and over a long period by self-measurement at home. Therefore, it is necessary to standardize the conditions of measurement. Among the several issues regarding these conditions, how many times measurements should be taken on each occasion has not yet been resolved [6]. The American and Japanese guidelines propose two measurements on each occasion [7, 8]. The European guideline proposes three measurements on each occasion [9]. Many previous studies have shown that the BP of the second measurement was lower than that of the first measurement [10–16]. However, it is not clear whether this tendency is a consistent finding for each subject over a long period. In addition, the superiority of the prognostic value of two measurements is not consistent.

Although it is extremely important to manage BP control based on HBP in the medical treatment of chronic kidney disease (CKD) patients, the details regarding the use of two measurements of HBP in these patients are not clear in clinical practice. The objective of this study is to clarify the actual state of two measurements of HBP on each occasion in CKD patients.

Subjects and Methods

Patients

We enrolled 175 patients treated at our department between May 2012 and February 2013 who met the eligibility criteria. As a first criterion for inclusion, CKD patients had to have been treated for ≥ 6 months at our clinic. CKD was diagnosed either by the presence of overt proteinuria or by decreased kidney function according to an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m² [17]. As a second criterion, the patients' HBP measurements had to have already been obtained at regular intervals before participation in this study. We excluded those patients who started dialysis therapy or who had atrial fibrillation.

Of the 175 patients, 122 were men. The mean age at the time of HBP data collection was 69 ± 11 years (range 28–98). The underlying renal diseases were as follows: chronic glomerulonephritis ($n = 63$), nephrosclerosis ($n = 57$), diabetic nephropathy ($n = 45$), polycystic kidney disease ($n = 5$), tubulointerstitial nephritis ($n = 2$), and reflux nephropathy ($n = 3$). These diseases were diagnosed on the basis of the medical history and renal biopsy findings.

The mean baseline serum creatinine level was 2.7 ± 2.0 mg/dl (range 0.57–10.70), and the mean eGFR was 28.7 ± 19.7 ml/min/1.73 m² (range 4.2–81.5; CKD stages 2, 3, 4, and 5: $n = 18, 45, 60$, and 52 , respectively), calculated by the following formula for Japanese patients: $194 \times \text{Cr}^{-1.094} \times \text{age}^{-0.287}$ ($\times 0.739$ for women) [18]. The mean creatinine clearance rate was 37.9 ± 29.6 ml/min (range 5.1–174.0; $n = 150$), the mean urinary protein excretion rate was 1.28 ± 1.53 g/day (range 0–9.1; $n = 150$), and the mean sodium excretion rate was 144 ± 65 mEq/day ($n = 150$). The mean hemoglobin level was 12.2 ± 1.7 g/dl, and the mean serum uric acid level was 7.2 ± 1.6 mg/dl. The mean body mass index was 24.1 ± 3.9 .

HBP Measurements and Data Collection

HBP was measured according to the guidelines for HBP measurement of the Japanese Society of Hypertension (JSH) [19]. BP was measured using oscillometric arm devices in a seated position after at least 1 min of rest. It was measured twice, with an interval of 1 min between measurements – in the morning within 1 h after waking before dosing, and in the evening just before bedtime. The values of the two measurements were recorded at each of these time points. The patients recorded 28 BP readings as described above over 7 days preceding their clinic visit. The first measurements (1st BP) and the second measurements (2nd BP) of the morning and evening BP values taken over 7 days were averaged for each patient. The differences between the 1st BP and the 2nd BP (2nd – 1st BP) were obtained and averaged for each patient. In 56 patients, HBP data were recorded with the same method after 1.6 ± 0.8 months (range 1–4) without changes in antihypertensive drugs.

This study was approved by the Ethics Committee of the Tokyo Medical University (No. 2924), and all patients provided written informed consent to use their clinical data in this study.

Treatment at the Time of Data Collection

We treated the patients according to the guidelines of the JSH [19]. Antihypertensive drugs were selected according to the guidelines of the JSH as well [20]. The numbers of antihypertensive drugs taken by the

Table 1. BP and heart rate parameters

	1st	2nd	2nd – 1st	p
Morning SBP, mm Hg	135.7±14.9	133.4±14.5	–2.3±4.1	<0.001
SD of morning SBP, mm Hg	7.3±3.5	7.2±3.5		0.62
Morning DBP, mm Hg	76.5±10.3	76.1±10.0	–0.4±2.6	0.005
SD of morning DBP, mm Hg	4.7±2.1	4.6±2.3		0.27
Evening SBP, mm Hg	130.1±14.6	127.9±14.7	–2.3±4.4	<0.001
SD of evening SBP, mm Hg	8.6±4.8	8.1±4.3		0.28
Evening DBP, mm Hg	71.6±10.2	71.5±9.9	–0.2±2.5	0.06
SD of evening DBP, mm Hg	5.3±2.5	5.2±2.6		0.21
Morning heart rate, bpm	69.7±10.5	68.6±10.0		<0.001
Evening heart rate, bpm	72.1±10.0	71.0±10.0		<0.001

subjects at the time of HBP data collection were as follows: 0 (n = 14), 1 (n = 39), 2 (n = 58), 3 (n = 43), and ≥4 (n = 21). The types of antihypertensive drugs taken by the subjects were as follows: angiotensin receptor blockers (n = 130), calcium channel blockers (n = 127), α_1 -blockers (n = 36), angiotensin-converting enzyme inhibitors (n = 27), $\alpha\beta$ -blockers (n = 21), and β_1 -blockers (n = 12). Furosemide, thiazide, and an aldosterone blocker were given to 34, 18, and 5 patients, respectively.

Statistical Analysis

Data are expressed as means ± SD. p values <0.05 were considered to represent statistically significant differences. Changes in BP parameters between measurements were analyzed by the Wilcoxon signed-rank test. The values of 2nd – 1st BP at the first time point and those at the second time point were analyzed by the Mann-Whitney test. Correlations between BP variables were analyzed by the Pearson correlation coefficient. Multiple regression analysis was performed to identify the independent variables associated with 2nd – 1st BP. Statistical analyses were performed using SPSS version 21 (IBM, Tokyo, Japan).

Results

BP Parameters

Table 1 shows the BP and heart rate parameters. The 2nd – 1st morning systolic/diastolic BP (SBP/DBP) and 2nd – 1st evening SBP/DBP differences were $-2.3 \pm 4.1/-0.4 \pm 2.6$ and $-2.3 \pm 4.4/-0.2 \pm 2.5$ mm Hg, respectively. The 2nd morning SBP, morning DBP, and evening SBP values were significantly lower than their respective 1st BP measurements. No significant changes were found between the SD values of 1st BP and those of 2nd BP.

Distributions of 2nd – 1st SBP

Table 2 shows the distribution of the numbers of patients and measurements according to 2nd – 1st SBP. The distribution of the numbers of patients was based on the average values of 2nd – 1st SBP during 7 days. The distribution of the numbers of measurements was based on each value of 2nd – 1st SBP in the whole patient population during 7 days. The greatest proportion of 2nd – 1st SBP differences lay within the range of 0 to –4.9 mm Hg (patients: morning 52.0%, evening 45.1%; measurements: morning 34.6%, evening 30.4%). The proportion of patients whose 2nd – 1st SBP differences were >0 mm Hg was 26.3% in the morning and 30.9% in the evening, respectively. The proportion of measurements >0 mm Hg for 2nd – 1st SBP was 31.7% in the morning and 34.2% in the evening, respectively.

Table 3 shows the distribution of patient numbers according to 2nd – 1st SBP during 7 days; 80 patients (45.7%) had days with a difference ≤–5 mm Hg and days with a difference ≥5 mm Hg in 2nd – 1st morning SBP.

Table 2. Distribution of the differences between 1st and 2nd measurements of SBP (2nd – 1st SBP)

	Morning (n = 175 patients)	Evening (n = 175 patients)	Morning (n = 1,195 measurements)	Evening (n = 1,189 measurements)
≤–10 mm Hg	6 (3.4%)	11 (6.3%)	168 (14.1%)	186 (15.6%)
–5 to –9.9 mm Hg	32 (18.3%)	31 (17.7%)	234 (19.6%)	231 (19.3%)
0 to –4.9 mm Hg	91 (52.0%)	79 (45.1%)	414 (34.6%)	363 (30.4%)
0.1 to 4.9 mm Hg	40 (22.8%)	43 (24.6%)	209 (17.5%)	219 (18.3%)
5 to 9.9 mm Hg	5 (2.9%)	11 (6.3%)	99 (8.3%)	115 (9.6%)
≥10 mm Hg	1 (0.6%)	0 (0.0%)	71 (5.9%)	75 (6.3%)

Table 3. Distribution of patient numbers according to 2nd – 1st SBP during 7 days

<i>2nd – 1st morning SBP</i>	
Patients who had days with a difference ≤–5 mm Hg	69 (39.4%) ^a
Patients who had days with a difference ≤–5 mm Hg and days with a difference ≥5 mm Hg	80 (45.7%) ^b
Patients who had days with a difference ≥5 mm Hg	15 (8.6%) ^c
Patients who had days with a difference within the range of >–5 and <5 mm Hg	11 (6.3%) ^d
<i>2nd – 1st evening SBP</i>	
Patients who had days with a difference ≤–5 mm Hg	65 (37.1%)
Patients who had days with a difference ≤–5 mm Hg and days with a difference ≥5 mm Hg	79 (45.1%)
Patients who had days with a difference ≥5 mm Hg	18 (10.3%)
Patients who had days with a difference within the range of >–5 and <5 mm Hg	13 (7.5%)

^a 44 patients had days with a difference ≤–5 mm Hg in the evening. ^b 55 patients had days with a difference ≤–5 mm Hg and days with a difference ≥5 mm Hg in the evening. ^c 10 patients had days with a difference ≤–5 mm Hg in the evening. ^d 9 patients had days with a difference within the range of >–5 and <5 mm Hg in the evening.

Correlations between 2nd – 1st SBP and Clinical Parameters

There was a weak but significant correlation between 2nd – 1st morning SBP and 2nd – 1st evening SBP ($r = 0.30$, $p < 0.001$). There was no significant difference between 2nd – 1st morning SBP in males and that in females (-2.2 ± 4.3 vs. -2.7 ± 3.6 mm Hg, $p = 0.73$). There were no significant differences in 2nd – 1st morning SBP between the patients with chronic glomerulonephritis, those with nephrosclerosis, and those with diabetic nephropathy (data not shown). There were no significant correlations between age, eGFR, the number of antihypertensive drugs, and 2nd – 1st morning SBP (data not shown).

The multivariate regression analysis of 2nd – 1st morning SBP as a dependent variable showed that 1st morning SBP ($\beta = -0.27$, $p = 0.01$) was the only significant determinant, whereas age, sex, eGFR, body mass index, diabetes mellitus, and the number of antihypertensive drugs were not ($R^2 = 0.07$).

Variability of 2nd – 1st BP

The mean SD values of 2nd – 1st morning and evening BP were $6.2 \pm 3.4/4.3 \pm 2.4$ and $6.5 \pm 3.6/4.6 \pm 2.9$ mm Hg, respectively. The mean SD value of 2nd – 1st morning SBP was not significantly associated with 1st morning SBP and 2nd – 1st morning SBP ($r = -0.12$ and $r = -0.05$, $p = 0.09$ and $p = 0.55$). However, it was significantly associated with the mean SD value of 1st morning SBP ($r = 0.64$, $p < 0.001$) (fig. 1). The mean SD value of 2nd – 1st evening SBP

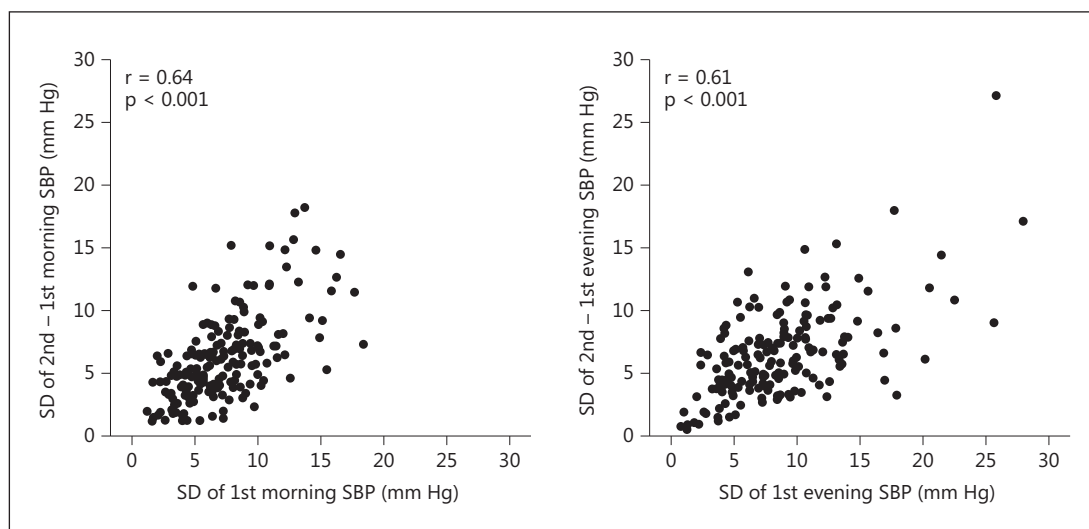


Fig. 1. Correlations between SD values of 1st SBP and SD values of 2nd – 1st SBP during 7 days.

had similar results. The multivariate regression analysis of the mean SD value of 2nd – 1st morning SBP as a dependent variable showed that the mean SD value of 1st morning SBP ($\beta = 0.65$, $p < 0.001$) was a significant determinant and female sex was a borderline significant determinant ($\beta = 0.12$, $p = 0.05$), whereas age, eGFR, body mass index, diabetes mellitus, and the number of antihypertensive drugs were not ($R^2 = 0.66$).

Reproducibility of 2nd – 1st BP

In the 56 patients who recorded their HBP data by the same method after 1.6 ± 0.8 months, there were no significant differences between BP values at the first time point and those at the second time point ($137.3 \pm 16.4/77.5 \pm 11.3$ mm Hg in the morning at the first and $138.7 \pm 17.6/78.1 \pm 10.8$ mm Hg in the morning at the second time point; $131.3 \pm 16.8/72.7 \pm 10.7$ mm Hg in the evening at the first and $132.8 \pm 16.3/73.2 \pm 10.6$ mm Hg in the evening at the second time point). There was no significant difference between 2nd – 1st morning BP at the first time point and those at the second time point ($-2.9 \pm 4.3/-0.6 \pm 2.6$ and $-2.2 \pm 4.1/-0.5 \pm 2.5$ mm Hg; SBP: $p = 0.41$; DBP: $p = 0.59$). The 2nd – 1st evening BP showed similar results (data not shown). There was a significant correlation between 2nd – 1st SBP at the first time point and those at the second time point (morning: $r = 0.35$, $p = 0.008$; evening: $r = 0.46$, $p < 0.001$).

Discussion

The present study showed the various differences in 2nd – 1st BP for each subject during 7 days. Although the 2nd SBP was 2–3 mm Hg lower than the 1st SBP in the population as a whole, about 30% of the patients had 2nd – 1st SBP >0 mm Hg. The results of our study agree with those of the previous studies, in which the mean values of 2nd measurements were 2–3/1–2 mm Hg lower than the mean values of 1st measurements on each occasion [10–16]. However, the details regarding the differences between the two measurements were not clarified in these previous studies. One of these studies showed that 30–40% of healthy individuals had higher 2nd measurement than 1st measurement values [11]. In the Home Blood

Pressure Measurement with Olmesartan Naive Patients to Establish Standard Target Blood Pressure (HONEST) study, the greatest proportion of 2nd – 1st morning SBP differences lay within the range of 0 to –4.9 mm Hg (43.1%) in 22,162 patients with essential hypertension [16]. The proportion of patients whose 2nd – 1st morning SBP differences were >0 mm Hg was 26.3%. Only 6.8% of the included patients had renal diseases, and the eGFR was 72 ± 20 ml/min/1.73 m². Although this study obtained averaged BP values from only 2 days, the distribution of patients according to BP changes was very similar to that of the present study. In the present study, no significant association between eGFR and 2nd – 1st morning SBP was found in the multivariate regression analysis. Thus, the presence of CKD might not affect the changes of BP.

One previous study showed the superiority of the 2nd BP measurement for prognosis or an association with target organ damage [15]. On the other hand, some studies have shown similar values between two measurements [13, 14]. Other studies have shown the prognostic value of one BP measurement on each occasion [4, 5, 21]. From these studies, the prognostic value of two measurements cannot be consistently derived. Further studies are necessary to clarify whether continuous double measurement is more beneficial than continuous single measurement with regard to the management of BP control.

In the present study, the 1st SBP was the only significant determinant of 2nd – 1st BP in the multivariate regression analysis. We could not identify the factors related to the changes of BP. However, many behavioral and physiological factors associated with short-term BP variability might influence changes of BP [22]. Increased sympathetic activity, decreased baroreflex activity, and arterial stiffness might be possible factors involved in the changes of BP in multiple measurements in the same way as the short-term BP variability assessed by ambulatory BP monitoring. Further studies are necessary to identify the factors related to changes of BP in multiple measurements.

The SD values of 2nd – 1st BP might represent as an index of short-term BP variability. Data regarding the variability of 2nd – 1st BP are scarce. In the Finn-Home Study, old age, female sex, history of cardiovascular disease, and high HBP were independent determinants of greater variability in 2nd – 1st measurements of HBP [23]. In the present study, female sex was a borderline significant determinant of SD values of 2nd – 1st morning SBP in the multivariate regression analysis. In addition, the SD values of 2nd – 1st SBP were significantly associated with the SD values of 1st SBP both in the morning and in the evening. To the best of our knowledge, there are as yet no studies regarding the relation between these variabilities. From these results, variability in 2nd – 1st measurements might be significantly associated with day-by-day variability. In the Finn-Home Study, variability in diastolic 2nd – 1st measurement of BP predicted cardiovascular events as well as morning day-by-day diastolic BP variability. Therefore, variability in 2nd – 1st measurements might have a clinical significance similar to that of day-by-day variability [23]. Further studies are necessary to clarify the clinical significance of the relation between these variabilities.

The present study assessed the reproducibility of 2nd – 1st BP. One previous study has shown the agreement of the 1st measurement and the 2nd measurement between separated periods in healthy volunteers [12]. It is not clear whether this tendency would be applicable to treated hypertensive patients. Although the correlation was weak in the present study, some populations might have characteristics which entail a consistent change of BP during two measurements.

This study has some limitations. First, the study cohort was small, possibly limiting the statistical power. Also, only patients who continued HBP measurements regularly were included in the study; thus, a bias in the selection of the study population cannot be completely ruled out. Second, although BP was measured twice with an interval of 1 min between measurements, the condition during the interval between measurements was not uniform.

In conclusion, although the 2nd BP has lower values than the 1st BP in the population as a whole, various differences between two measurements were found for each subject during 7 days in patients with CKD. 2nd – 1st BP variability was significantly associated with day-by-day variability. Further studies are necessary to clarify the factors affecting the BP change between two measurements, and to clarify the significance of two measurements of HBP on each occasion in clinical practice.

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